REMARKS

Claims 1-11, 13-14, 17-18, 21 and 24-27 are pending. Claims 22, 23 and 28-49 are canceled. Claims 12, 15-16, and 19-20 are withdrawn from consideration with the understanding that said claims will be reintroduced upon allowance of a generic claim.

1. Claim Objections

Claims 1-11, 13-14, 17-18, 21, and 24-27 are objected to by the Examiner because of the following informalities.

Claim 1, throughout and claim 2, lines 1-2 read "heterogeneous sample of peptides, or protein or peptide fragments,.." Applicants have amended the claims to recite "heterogeneous sample of peptides, proteins, protein fragments, or peptide fragments" is suggested.

Claim 1, throughout; claim 7, throughout; claim 9, line 2; claim 10, line 3; claim 21, line 2; and claim 24, line 2, read "...peptide(s), or protein or peptide fragment(s)..." Applicants have amended the claims to recite "heterogeneous sample of peptides, proteins, protein fragments, or peptide fragments."

In claim 1, line 10, "heterogenous" should read "heterogeneous." Applicants have amended the claim to read "heterogeneous."

Claims 2-6 and 14 have "claim" capitalized within the body of the claim. Claims 2-6 and 14 have been amended to have "claim" in lower case.

Claim 26 contains "~~a~~" from a previous amendment (i.e. August 25, 2006; line 2). Claim 26 has been amended to delete "~~a.~~"

Claim 27, lines 2-3 reads "heterogeneous fragmented or unfragmented samples of peptides, or protein or peptide fragments..." Claim 27 has been amended to recite "heterogeneous fragmented or unfragmented samples of proteins, peptides, protein fragments or peptide fragments."

2. The Claims Comply With the Written Description Requirement

Claims 1-11,13-14,17-18, 21, and 24-27 are rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement. According to the Examiner, the claims contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

The Examiner maintains that the claim amendment received on November 19, 2007 added the following text to independent claim 1: "wherein more than one peptide, protein or peptide fragment binds to each defined location on the array," and that Applicants failed to point out support for the claim amendment in the originally filed specification.

Applicants submit that support for the claim amendment can be found, for example, in [0017] of the specification which states that "a heterogeneous class of peptides or proteins will bind to specific binding molecule due to the presence of a motif common to all members of a particular class." Applicants maintain that "a heterogeneous class of peptides or proteins" implies that more than one peptide or protein may bind to a defined location on the array. Therefore, the claims comply with the written description requirement.

3. The Claims as Amended Are Definite

Claims 3, 6, 8, 14, 25, and 26 are rejected by the Examiner under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 3 and 6 are said to recite the limitation "the heterogeneous sample of fragments" in lines 2, however, according to the Examiner there is insufficient antecedent basis for this limitation in the claim.

Claims 8 and 14 are said to recite the limitation "the sample" in line 1 and line 3, respectively, however, according to the Examiner there is insufficient antecedent basis for this limitation in the claim.

Claim 14 is said to recite the limitation "the unfragmented sample" in lines 3 and 5, however, according to the Examiner, there is insufficient antecedent basis for this limitation in the claim.

Claim 14 is also said to recite the limitations "the peptides" and "the proteins or peptides" in lines 3 and 5, respectively, however, accoridng to the Examiner, there is insufficient antecedent basis for this limitation in the claim.

Claims 25 and 26 are said to recite the limitation "the parent protein or peptide" in lines 2, however, according to the Examiner, there is insufficient antecedent basis for this limitation in the claim.

Claims 25 and 26 are said to recite the limitation "the unfragmented heterogeneous sample" in line 3, however, according to the Examiner there is insufficient antecedent basis for this limitation in the claim.

Claim 26 is said to recite the limitation "the detected protein or peptide fragment" in lines 3-4, however, according to the Examiner there is insufficient antecedent basis for this limitation in the claim.

Applicants have amended the claims to correct antecedent basis, therefore, withdrawal of the claim rejections under 35 U.S.C. §112 is respectfully requested.

4. The Claims Are Not Obvious in View of Minden and Nelson or in View of Minden and Barry

Claims 1-11,13-14,17-18, 21, and 24-27 are rejected under 35 U.S.C. §103(a) as being unpatentable over Minden et al. WO 02/086081 A2 ("Minden") and Nelson et al. U.S. Patent 6,887,713 ("Nelson").

According to the Examiner, Minden et al. teach methods of identifying a protein via assigning (i.e. separating) binding reagents to designated locations on an array, detecting the binding patterns, and comparing the binding pattern to a reference set (i.e. characterizing; please refer to the abstract, paragraphs [0005-0012], [0028-0032], [0035-0044], [0072-0074], [0077], [00117], Figures 1-11, and Table 1). In addition, Minden is said to further teach (i) that the molecular weight or mass of the binding reagents can be determined and that spectrometry can be utilized; (ii) that more than one protein can have the same epitope thus the common epitopes (i.e. more than one) would bind to the same defined location; (iii) that the total protein content of a cell or tissue can be utilized as the protein mixture; (iv) that the protein mixture can be fragmented with various chemical or enzymatic methods including trypsin; (v) that trypsin cleavage forms a peptide or epitope (i.e. motif) with C-terminal lysine or arginine residues; (vi) that the peptides or epitopes (i.e. motifs) can be at least three amino acids in length and can have at least two variable amino acids; (vii) that arrays can have different binding molecules at spatially addressable locations which bind to different binding reagents; (viii) that the protein mixture may comprise all (i.e. at least 10% of the peptides) of the proteins and that the epitopes cover the binding mixture; (ix) that the array can have 2-100 different proteins; (x) that the binding reagents can be antibodies; (xi) that the proteins are compared to a reference set (i.e. characterizing; (xii) that the reference set can include prediction about binding based on the predicted digests of a protein mixture; (xiii) that various binding reagents can be compared to a reference set or to other binding reagents.

According to the Examiner, although Minden does not specifically teach determining the abundance of the proteins by the use of desorption mass spectrometry or collision induced dissociation mass spectrometry, for present claims 1, 24, and 26, Nelson teaches analyzing complex biological mixtures utilizing "lab-on-a-chip" (i.e. chip-based microarrays) and MALDI-TOF (i.e. combination of both desorption mass spectrometry and collision induced

dissociation mass spectrometry) wherein the proteins are quantified (i.e. abundance), internal reference standards are utilized, and determining the amount (i.e. abundance) of the proteins. According to the Examiner, the claims would have been obvious because the substitution of one known element (i.e. mass spectrometry providing mass information only) for another (i.e. mass spectrometry providing both mass and abundance information; MALDI-TOF) would have yielded predictable results to one of ordinary skill in the art at the time of the invention and/or (b) the claim would have been obvious because a particular known technique (i.e. MALDI-TOF utilized to determine mass and abundance of proteins) was recognized as part of the ordinary capabilities of one skilled in the art. See *KSR Int'l Co. v. Teleflex Inc.*, 127 S. Ct. 1727, 1741 (2007).

The rejection of Claims 1-11,13-14,17-18, 21, and 24-27 is maintained by the Examiner under 35 U.S.C. §103(a) as being unpatentable over Minden et al. WO 02/086081 A2 (filing date April 22, 2002) and Barry et al. WO 0225287 (filed September 19, 2001). According to the Examiner, Minden teaches methods of identifying a protein via assigning (e.g. separating) binding reagents to designated locations on an array, detecting the binding patterns, and comparing the binding pattern to a reference set. Minden is alleged to further teach (i) that the total protein content of a cell or tissue can be utilized as the protein mixture; (ii) that the protein mixture can be fragmented with various chemical or enzymatic methods including trypsin; (iii) that trypsin cleavage forms a peptide or epitope (e.g. motif) with C-terminal lysine or arginine residues; (iv) that the peptides or epitopes (e.g. motifs) can be at least three amino acids in length and can have at least two variable amino; (v) that arrays can have different binding molecules at spatially addressable locations which bind to different binding reagents; that the protein mixture may comprise all (e.g. 100%) of the proteins and that the epitopes cover the binding mixture; (vi) that the array can have 2-100 different proteins; (vii) that the binding reagents can be antibodies; (viii) that the proteins can be compared to a reference set; (ix) that the molecular weight or mass of the binding reagents

can be determined and that spectrometry can be utilized; (x) that the reference set can include prediction about binding based on the predicted digests of a protein mixture (e.g. unfragmented); and (xi) that various binding reagents can be compared to a reference set or to other binding reagents.

The Examiner alleges that, although Minden does not specifically teach determining the abundance of the proteins or the use of desorption mass spectrometry or collision induced dissociation mass spectrometry, Barry teaches methods of (i) determining the binding and mass of trypsin digested proteins (including antibodies) from a cell (including phage) or tissue sample immobilized on an array (please refer to the abstract, pages 2-6, 21-30, Figures 3-6 and 8-10, Examples 2-3); (ii) determining the abundance of proteins via MALDI-TOF; MALDI-TOF (matrix assisted laser desorption ionization-time of flight) mass spectrometry (e.g. combination of both desorption mass spectrometry and collision induced dissociation mass spectrometry or CID); and (iii) determining the abundance of the protein.

Applicants maintain that the present invention relates to a method for proteomic analysis of a heterogeneous sample of proteins, or protein or peptide fragments by *separating the sample into heterogeneous classes* at spaced apart locations on an array wherein no advanced knowledge of the identity of individual proteins in a protein sample is required in order to perform the method of the present invention. Additionally, the method of the invention recites a step that includes a determination of the *mass* and *abundance* of peptides, or protein or peptide fragments, in the heterogeneous classes that are bound to the array. Applicant asserts that there is nothing in Minden to suggest that *quantification of proteins* in the array-bound heterogeneous classes is desirable, *much less possible*.

According to the Examiner, although Minden may not specifically teach determining the abundance of the proteins, Nelson and Barry provide an abundance determination step to apply to Minden's method. In this regard, it is critical to note that Nelson discloses " a method and device for the capture and subsequent digestion or derivatization of ***an analyte***"

(See, col. 4, lines 41-43). Further, as depicted in Figure 1 of Nelson, the analyte appears to be a *single homogeneous molecule*. Further, as indicated previously, Barry only teaches a method of proteomic analysis *wherein each binding reagent corresponds to one protein* and requires advanced knowledge of proteins in the sample in order to generate an appropriate array of binders. In other words, Barry, like Nelson, only teaches the determination of abundance wherein the analysis is applied to *homogeneous* classes of array-bound proteins.

Both the teachings of Barry and Nelson are in contrast to the present invention which relates to a method of determining the mass and abundance of a heterogeneous class of array-bound peptides, or protein or peptide fragments. Applicants maintain that, indeed, it is the basis of the present invention to provide a means for *complex sample evaluation* with relatively small arrays.

Applicants assert that the Examiner has failed to site a single reference where the abundance of a heterogenous sample of proteins is measured. Thus, one of ordinary skill in the art, would not have had a reasonable expectation of success that a heterogeneous class of proteins bound to an array could be successfully quantified. Therefore, a *prima facia* case of obviousness has not been established. In light of these remarks, Applicant respectfully requests that the obviousness rejections be withdrawn.

CONCLUSION

In view of the foregoing amendments and remarks, it is believed that the subject claims are in condition for allowance, which action is earnestly solicited. If, in the opinion of

the Examiner, a telephone conference would expedite prosecution of the subject application, the Examiner is invited to call the undersigned attorney.

Respectfully submitted,

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